

correspondence

Like it or not, life-extension research extends beyond biogerontology

Lord Kelvin, once President of the Royal Society, notoriously asserted in 1895 that "Heavier-than-air flying machines are impossible." Ignoring such unenviable precedents, in this issue of *EMBO reports*, Warner and 27 other biogerontologists dismiss strategies for engineered negligible senescence (SENS) as 'scientifically' unrealistic (Warner *et al.*, 2005). Like Kelvin, they forget that engineering—of which life extension will be an example, as all medicine is—differs profoundly from science in its goals, methods and skills.

Illustrating this, Warner *et al.* accuse me of "[t]reating arguments and proposals that are not backed up by scientific evidence as though they were scientific ideas", but they are wrong in both fact and logic. Regarding logic, they stress my failure to note that no SENS intervention—in isolation—has ever been shown to extend any organism's lifespan. I do not recall Henry Ford alerting potential customers that the components of a car—in isolation—remain obstinately stationary when burning petrol is poured on them, nor do I recall his being castigated for this omission. Similarly, if engineers followed scientists' lead in regarding the most direct evidence as the most valuable, we would still be trying to fly by flapping. This failure to appreciate a key tenet of technology would be shocking enough if it were merely tunnel vision, but it is worse, because I have highlighted the error in the very articles (de Grey, 2003, 2005) that Warner *et al.* cite and thereby imply that they have read.

Concerning fact, their knowledge of SENS is woeful. They "promise that we will be impressed" by evidence that some aspects of ageing can be reversed by phenacyldimethylthiazolium chloride—but this has been published repeatedly, leading

to clinical trials (Kass *et al.*, 2001). The modest benefit from stimulating IL-7 has long been acknowledged in SENS, even in an article (de Grey *et al.*, 2002) cited "for details" in the legend to the table (de Grey, 2003) that was apparently Warner *et al.*'s sole source for what SENS proposes. SENS has long subsumed immunosenescence under cell depletion and cell senescence, the latter defined as the persistence of non-dividing but harmful cells: the role of, for example, T-cell clonal expansions is thus incorporated. SENS has never claimed to be complete in every detail but nor, at their outset, did the Apollo programme, the Human Genome Project or any other comparably far-reaching endeavour. On the contrary, the coherent structure of SENS actively aids its refinement in the light of new data and highlights what new knowledge is most needed—another ubiquitous aspect of engineering that Warner *et al.* overlook. They mention side effects of deleting telomerase genes throughout the body, insinuating that WILT—the relevant SENS component—ignores these, when in fact it has always addressed them (de Grey *et al.*, 2004). And so on. Ageing indeed possesses Menckenesque complexity, but SENS is not simple.

Who is to blame for Warner *et al.*'s ignorance of what they are dismissing? A clear answer emerges when I compare their names with the list of equally eminent individuals who have let me know that they were asked to be co-authors but declined: no signatories attended my recent SENS2 conference, whereas many refusers did. Have Warner *et al.* considered that the refusers might know some relevant facts that they do not, some of which may have been gleaned from my publications and conferences? This is sadly characteristic of biogerontology, which defines itself so narrowly as to exclude swathes of biology that may well underpin future life extension therapies. The proceedings of SENS2 will appear shortly in *Rejuvenation Research*; all biogerontologists will find it valuable.

What does this mean for SENS's likelihood of success (initially in mice) within the timeframe I have predicted? Warner *et al.* presumably accept that the likely timeframe for

any technological achievement depends on how far towards it prior work has progressed, hence ignorance of prior work results in unwarranted overoptimism. It is thus odd that they so confidently deprecate SENS's chances despite having neglected to familiarize themselves with the experimental work, amply cited in my publications, that underpins SENS. Since public research funding depends enormously on mainstream acceptance of the likelihood of success, their exhortation to me to seek such funding is, likewise, transparently rhetorical.

Warner *et al.* are avowedly in the business of saving lives, just like me: dogma must not obstruct our common cause. They do not challenge my arguments that adherence to biologically and politically naive rhetoric is precisely why gerontology continues to have such trouble impressing policy-makers, yet they steadfastly defend that rhetoric as if somehow one more push will change everything. I offer no apology for using media interest in life extension to make the biology of ageing an exception to Planck's observation that science advances funeral by funeral: lives, lots of them, are at stake.

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